CLAIMS

What is claimed is:

1. An antisense oligonucleotide for inhibiting expression of an aldehyde dehydrogenase gene in a cell, the oligonucleotide comprising at least 12 nucleotide residues and having a sequence selected such that the oligonucleotide anneals in the cell with a portion of an RNA molecule corresponding to the gene, wherein the portion comprises a GGGA motif, whereby the oligonucleotide inhibits expression of the gene in the cell.

2. The oligonucleotide of claim 1, wherein the gene is an ALDH2 gene.

3. The oligonucleotide of claim 2, wherein the gene is a human gene.

4. The oligonucleotide of claim 3, wherein the RNA molecule corresponds to the ALDH2-1 allele of the ALDH2 gene.

5. The oligonucleotide of claim 3, wherein the sequence of the oligonucleotide is homologous with or complementary to at least 12 nucleotide residues of one of SEQ ID NOs: 108 and 110.

6. The oligonucleotide of claim 1, wherein the oligonucleotide comprises from 12 to 2000 nucleotide residues.

7. The oligonucleotide of claim 1, wherein the oligonucleotide comprises from 12 to 50 nucleotide residues.

8. The oligonucleotide of claim 7, wherein the oligonucleotide comprises from 14 to 30 nucleotide residues.

9. The oligonucleotide of claim 7, wherein the oligonucleotide comprises from 16 to 23 nucleotide residues.

10. The oligonucleotide of claim 1, wherein the oligonucleotide is completely complementary to the portion.

11. The oligonucleotide of claim 1, wherein the oligonucleotide is at least 90% complementary to the portion.

12. The oligonucleotide of claim 1, wherein the oligonucleotide is at least 95% complementary to the portion.

13. The oligonucleotide of claim 1, wherein the sequence of the oligonucleotide comprises a sequence selected from the group consisting of SEQ ID NOs: 98, 107, 109, and 111.

14. The oligonucleotide of claim 13, having the sequence SEQ ID NO: 98.

15. The oligonucleotide of claim 13, having the sequence SEQ ID NO: 111.

16. The oligonucleotide of claim 1, wherein the RNA molecule is the primary transcript of the gene.

17. The oligonucleotide of claim 1, wherein the RNA molecule is an mRNA of the gene.

18. The oligonucleotide of claim 1, wherein at least one linkage between the nucleotide residues of the oligonucleotide is a non-phosphodiester linkage.

19. The oligonucleotide of claim 18, wherein at least one linkage between nucleotide residues of the oligonucleotide is a phosphorothioate linkage.

20. The oligonucleotide of claim 18, wherein every linkage between nucleotide residues of the oligonucleotide is a phosphorothioate linkage.

21. A pharmaceutical composition for inhibiting expression of an aldehyde dehydrogenase gene in a cell, the composition comprising the oligonucleotide of claim 1 suspended in a pharmaceutically acceptable carrier.

22. A pharmaceutical composition for inhibiting expression of an aldehyde dehydrogenase gene in a cell, the pharmaceutical composition comprising a transcription vector for transcribing the oligonucleotide of claim 1 in the cell, the vector being suspended in a pharmaceutically acceptable carrier.

23. The method of claim 22, wherein the transcription vector is a plasmid.

24. The method of claim 22, wherein the transcription vector is a virus vector.

25. A method of decreasing ethanol tolerance in a human, the method comprising administering the oligonucleotide of claim 1 to liver cells of the human, whereby the oligonucleotide inhibits expression of the aldehyde dehydrogenase gene in the cells and decreases ethanol tolerance in the human.

26. The method of claim 25, wherein the oligonucleotide is administered to the cells by delivering the oligonucleotide to the bloodstream of the human.

27. The method of claim 25, wherein the oligonucleotide is administered to the cells by injecting a pharmaceutical composition comprising the oligonucleotide into the liver of the human.

28. The method of claim 25, wherein the oligonucleotide is administered to the cells by administering to the cells a transcription vector for transcribing the oligonucleotide in the cells.

29. The method of claim 28, wherein the transcription vector is a plasmid.

30. The method of claim 28, wherein the transcription vector is a virus vector.

31. A method of inhibiting ethanol intake by a human, the method comprising administering the oligonucleotide of claim 1 to liver cells of the human, whereby the oligonucleotide inhibits expression of the aldehyde dehydrogenase gene in the cells, decreases the ethanol tolerance of the human, and thereby inhibits ethanol intake by the human.

32. A method of decreasing the desire of a human to consume ethanol, the method comprising administering the oligonucleotide of claim 1 to liver cells of the human, whereby the oligonucleotide inhibits expression of the aldehyde dehydrogenase gene in the cells, thereby decreasing the ability of the human to metabolize acetaldehyde and increasing the non-desirability of ethanol consumption.

33. A polynucleotide for inhibiting aldehyde dehydrogenase activity in a cell, the polynucleotide encoding an exogenous ALDH2-2 allele operably linked with a promoter/regulatory region, whereby the ALDH2-2 allele is expressed in the cell when the polynucleotide is delivered to the interior of the cell, the ALDH2-2 gene product multimerizes with an endogenous aldehyde dehydrogenase subunit, and the activity of the endogenous aldehyde dehydrogenase is inhibited.

34. The polynucleotide of claim 33, wherein the cell is a human cell.

35. The polynucleotide of claim 34, wherein the cell is a liver cell.

36. The polynucleotide of claim 33, wherein the exogenous ALDH2-2 allele has the nucleotide sequence SEQ ID NO: 110 having an adenine residue at position 1543.

37. The polynucleotide of claim 33, wherein the exogenous ALDH2-2 allele is operably linked with an expression vector.

38. The method of claim 37, wherein the expression vector is a plasmid.

39. The method of claim 37, wherein the expression vector is a virus vector.

40. A pharmaceutical composition for inhibiting aldehyde dehydrogenase activity in a cell, the pharmaceutical composition comprising the polynucleotide of claim 33 suspended in a pharmaceutically acceptable carrier.

41. A method of decreasing ethanol tolerance in a human, the method comprising administering the polynucleotide of claim 33 to liver cells of the human, whereby

the ALDH2-2 allele is expressed in the cells, aldehyde dehydrogenase activity is inhibited in the cells, and ethanol tolerance decreases in the human.

42. A method of inhibiting ethanol intake by a human, the method comprising administering the polynucleotide of claim 33 to liver cells of the human, whereby the ALDH2-2 allele is expressed and inhibits aldehyde dehydrogenase activity in the cells, the ethanol tolerance of the human decreases, and ethanol intake by the human is thereby inhibited.

43. A method of decreasing the desire of a human to consume ethanol, the method comprising administering the polynucleotide of claim 33 to liver cells of the human, whereby the ALDH2-2 allele is expressed and inhibits aldehyde dehydrogenase activity in the cells, thereby decreasing the ability of the human to metabolize acetaldehyde and increasing the non-desirability of ethanol consumption.

44. A method of making an antisense oligonucleotide for inhibiting aldehyde dehydrogenase activity in a cell of a mammal, the method comprising

selecting a portion of an RNA molecule corresponding to an allele of the gene encoding the aldehyde dehydrogenase, wherein the portion comprises a GGGA motif and

synthesizing an oligonucleotide comprising at least 12 nucleotide residues and having a sequence selected such that it anneals in the cell with the portion,

whereby the oligonucleotide inhibits expression of the gene when it is administered to the interior of the cell.

45. An antisense oligonucleotide for inhibiting expression of a gene which encodes TNF-alpha in an animal, the oligonucleotide comprising from 12 to 50 nucleotide residues, wherein at least 90% of the nucleotide residues of the oligonucleotide are complementary to a region of an RNA molecule which corresponds to the gene, wherein the region comprises a GGGA motif.

46. The antisense oligonucleotide of claim 45, wherein the oligonucleotide comprises from 14 to 30 nucleotide residues, wherein the oligonucleotide comprises a TCCC motif, and wherein at least 95% of the nucleotide residues of the oligonucleotide are complementary to the region.

47. The antisense oligonucleotide of claim 45, wherein the oligonucleotide comprises from 16 to 21 nucleotide residues, comprises a TCCC motif, and is completely complementary to the region.

48. The antisense oligonucleotide of claim 45, wherein the animal is a human.

49. The antisense oligonucleotide of claim 48, wherein the antisense oligonucleotide is complementary to from 12 to 50 consecutive nucleotide residues of a region of the human TNF-alpha gene selected from the group consisting of regions I - XXII, the antisense oligonucleotide being complementary to at least one GGGA motif in the region.

50. An antisense oligonucleotide for inhibiting expression of a gene in an animal cell, the oligonucleotide being made by

identifying an RNA molecule corresponding to the gene, wherein the RNA molecule comprises a GGGA motif; and

synthesizing an oligonucleotide complementary to at least a portion of the RNA molecule, the portion comprising the motif,

whereby the oligonucleotide inhibits expression of the gene when it is administered to the interior of the cell.

51. A method of treating an animal afflicted with a disease or disorder characterized by the presence in an affected cell of the animal of an RNA molecule which corresponds to a gene, which RNA molecule comprises a region comprising a GGGA motif, the method comprising

providing an antisense oligonucleotide which is at least 90% complementary to the region; and

administering the oligonucleotide to the animal.

52. The method of claim 51, wherein the antisense oligonucleotide is completely complementary to the region.

53. The method of claim 51, wherein the RNA molecule is the primary transcript of the gene.

54. The method of claim 51, wherein the animal is a human.

55. The method of claim 54, wherein the gene encodes human TNF-alpha.

56. The method of claim 51, wherein at least one linkage between nucleotide residues of the oligonucleotide is a phosphorothioate linkage.

57. A method of inhibiting expression of a gene in an animal cell, the method comprising administering to the cell an antisense oligonucleotide which is complementary to a region of an RNA molecule corresponding to the gene, wherein the region comprises a GGGA motif.

58. A method of predicting the efficacy of an antisense oligonucleotide for inhibiting expression of a gene, the method comprising determining whether the antisense oligonucleotide is complementary to a region of an RNA molecule corresponding to the gene, wherein the region comprises a GGGA motif, whereby complementarity of the antisense oligonucleotide to the portion is an indication that the antisense oligonucleotide is efficacious for inhibiting expression of the gene.

59. A method of separating from a mixture of oligonucleotides an antisense oligonucleotide which is efficacious for inhibiting expression of a gene, the method comprising

contacting the mixture with a support linked to an oligonucleotide comprising a GGGA motif, whereby the efficacious antisense oligonucleotide associates with the support; and

separating the support from the mixture.